

Angina pectoris and coronary artery disease (CAD)

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Basic rules

- A history, clinical examination and some basic tests suffice for clinical diagnosis of stable angina pectoris in an elderly patient if revascularization is not being considered. Therapeutic trials often confirm the diagnosis.
- When the diagnosis is not clear, an exercise test is required for determining working capacity and often for insurance.
- When considering revascularization (Level of Evidence=A; Evidence Summary available on the EBM Web site), exercise test is usually the first examination.
- Serious or progressive (unstable) angina pectoris often requires urgent intervention in hospital without delay. Revascularization may be required.
- Prevention of coronary artery disease (CAD) includes effective reduction of the three "major" risk factors in addition to estimation of the total burden of risk to the individual¹. Both pharmacological therapy and patient education (Level of Evidence=B; Evidence Summary available on the EBM Web site) are effective.

Epidemiology

- CAD mortality of men under the age of 65 is three times that of women. In the older age group the mortality of both genders is equal. After 80 years of age the CAD mortality of women is twice that of men.
- Total CAD mortality remains unchanged but mortality under age 65 has fallen by 50% over the past two decades.

Clinical manifestations of CAD

- Angina pectoris (AP) is the most common reason for seeing a doctor.
- Dyspnoea on exertion may present before pain and may be misinterpreted. Other manifestations of CAD are syncope on exercise, arrhythmias, silent ischaemia, unstable angina, acute or chronic heart failure, myocardial infarction and sudden death.

Symptoms and clinical diagnosis of stable AP

- For differential diagnosis of chest pain see related EBM Guideline: **Differential diagnosis of chest pain** available on the EBM Web site
- Stable AP is a clinical diagnosis that means the precipitation of pain at a constant level of exercise characteristic for the patient. The pain is relieved after 10 minutes at rest and recurs without great daily variation in intensity. Variation is typical to nonischaemic chest pain.
- **The pain, pressure or ache of "typical angina pectoris"**
 - is precipitated by exertion
 - is worsened if the exertion is continued
 - is felt broadly in the middle of the chest (not in the cardiac apex)
 - may radiate to the throat, shoulders, epigastrium or back
 - is worsened by the cold, after a heavy meal or in static work
 - is relieved in a few minutes by rest or nitroglycerin.
- Only half of all patients have a typical presentation of the symptoms.
- The reliability of a history of angina pectoris is better in men. The probability of CAD in males over 55 with typical symptoms is 90%.
- Dyspnoea on exercise may be the earliest and the only symptom. Its cause is acute LV failure leading to pulmonary congestion.
- Pain and dyspnoea force the patient to slow down or stop walking. Patients with non-ischaemic pain are able to continue.
- Nocturnal angina is in most cases a symptom of gastro- oesophageal reflux.
- Some patients describe AP pain as burning which is why it may be misinterpreted as oesophageal pain.
- Ischaemic pain is usually predictable, precipitating at almost the same level of exertion. However, in some patients exercise tolerance may vary to some degree. Large variations are typical of non-ischaemic pain.
- The pain may be precipitated by psychological stress as this causes a rise in pulse-pressure product.
- The pain may be triggered by rapid onset of walking. After "warming up" the patient can again, "walk through his angina".
- The site of radiating pain does not vary in the same patient.
- After hard exercise the pain may remain for 15 minutes. More prolonged pain should be suspected as myocardial infarction or delayed recovery from an ischaemic insult (stunning).
- Worsening of stable angina is termed unstable angina. It requires urgent treatment and usually

hospitalization (See related EBM Guideline: **Unstable angina pectoris** available on the EBM Web site).

"Atypical pain" not suggesting coronary artery disease

- appears also at rest
- exercise tolerance is good despite pain
- continues for hours or days
- is provoked by breathing or chest movements
- feels sharp or burning
- is localized lateral to cardiac apex
- may be palpated at the thoracic wall
- is felt as palpitation or extrasystolia of a few seconds' duration
- is felt in the upper abdomen or below the left costal arch
- is not relieved with nitroglycerin after a few minutes.

Investigations

Physical investigation

- In most patients, physical signs reveal no pathology!
- Check blood pressure and heart rate, as pain often elevates both.
- Systolic bruit of a carotid or femoral artery suggests generalized atheromatous disease.
- Aortic murmur suggests aortic valve disease, which is frequently associated with CAD.
- S4 is common but silent and difficult to hear.
- S3 and a soft apical mitral murmur are signs of impaired cardiac function. They may also be a transient consequence of prolonged ischaemia.
- Palpation may reveal LVH. A patient with LVH is disposed to angina pectoris even when the coronary artery disease is mild.
- Pallor may suggest anaemia.
- Signs of heart failure may appear after prolonged ischaemia.

ECG

- The ECG is normal at rest in 30 - 50% of the patients. Recordings during an attack may be of value.
- Ischaemic ST-segment depression is sensitive but non-specific.
- Slightly prolonged (0.24 sec) PQ time is common in CAD.
- Patients with LVH often have ischaemia and AP (90%).
- LBBB suggests LVH and/or CAD.
- A previous infarction is a confident sign of CAD.
- Recording an ECG during an ischaemic attack is important. Reversible ST segment depression is strong evidence for CAD.
- Continuous monitoring in the CCU or by the Holter method may reveal silent ischaemia. This predicts CAD if the patient is at risk (Level of Evidence=B; Evidence Summary available on the EBM Web site).

Laboratory investigations

- Serum lipids, blood glucose and blood haemoglobin
- Chest x-ray: heart failure, valvular calcification, and other causes of chest pain -Even a slight rise in myocardial enzymes or markers after a prolonged angina attack is often a serious and signifies risk of infarction. Further examinations are necessary. (See related EBM Guideline: **Unstable angina pectoris** available on the EBM Web site)

Exercise tolerance test

- Angina pectoris is a clinical diagnosis that can be confirmed either by ECG during a spontaneous attack or by a therapeutic trial of nitroglycerin. Exercise test is not a routine examination.
- Exercise test has many limitations and problems of interpretation. The sensitivity and specificity are about 60 - 80%.
- The patient at risk, with a typical history of angina pectoris, ischaemic pain on a tolerance test and a simultaneous ischaemic ST segment, has a very high probability of CAD.
- An ischaemic ST (over 2 mm) even without angina (silent ischaemia) predicts CAD, especially if the patient is at risk. Silent ischaemia is most often revealed during CCU or Holter monitoring. Its significance is being debated and depends on the severity of CAD and the risk factors.
- Difficulties in the interpretation of an exercise test are met particularly with patients who have a low pre-test likelihood of CAD. A false-positive test result is most often obtained from sympathicotonic women under 50 years with atypical angina and without risk factors.
- A syndrome-X patient has typical angina pectoris and an abnormal exercise test result but normal coronary angiography and a benign prognosis. The syndrome is much more common among women under 50 years.
- A normal test result does not exclude CAD, however, the probability of moderate to serious CAD is very low.
- The patient should remain untreated until a diagnosis is made, with the exception of ASA administration. An exercise test gives valuable information about the severity of the diagnosed disease and the need for further investigations. After determining the severity of the disease, the patient must be treated optimally.

Radionuclide imaging (thallium scan) at rest or on exertion

- The sensitivity is somewhat higher; the specificity is equal to that of the exercise test.
- Valuable when the ECG is non-diagnostic because of concurrent abnormalities (LBBB, LVH, WPW).

Exercise echocardiography

- Detects wall motion abnormalities, especially in the left main vessel disease
- Optimal sensitivity up to 90%
- Important when ECG is non-diagnostic because of abnormalities

Coronary angiography

- Details in related EBM Guideline: **Coronary angiography and indications for CABG or angioplasty** available on the EBM Web site.
- Mainly an investigation preceding invasive therapy. Nowadays used increasingly for diagnosis.

Special diagnostic problems in women

- The specificity of "typical angina" symptoms is lower (about 50%) in premenopausal women.
 - Only about half of the women with typical angina pectoris have a significant ischaemic heart disease.
 - Under the age of 50, women experience chest pain more often than men. The pain is usually "atypical".
 - At an older age, the diagnostic sensitivity of the symptoms becomes as good as that in males (90%).
- The predictive value of exercise test is poorer in women because of a sympathicotonic ST change. The number of false-positive test results is high before menopause.
- An ischaemic ST change and yet a normal angiography finding (syndrome-X) are a much more common in premenopausal women compared with men.
- Under the age of 50, the specificity of radionuclide imaging and exercise echocardiography is higher than that of the traditional exercise test.

Treatment of risk factors

- It is difficult to obtain firm evidence on the benefits of treating a single risk factor. The conclusions are based on epidemiological observations and pathophysiology.
- Minimizing all risk factors to slow down atherosclerosis and prevent MI is considered important. Efficient secondary intervention usually includes ASA, beta-blocker, statin and discontinuation of smoking (Level of Evidence=D; Evidence Summary available on the EBM Web site)¹.
- Smoking should be discontinued and alcohol consumption should be limited to moderate amounts.
- Hypertension should be treated optimally. The target level of below 140/90 mmHg should be reached. According to the recent HOT Study² the optimum is 138/83 for CAD patients. Further lowering of diastolic pressure is neither more beneficial (except in diabetics) nor harmful. According to the present view, lowering diastolic pressure to below 90 mmHg does not increase the risk of infarction.
- Effective reduction of hyperlipidaemia is often possible only by using statins. Target levels:
 - total cholesterol level below 5.0 mmol/L
 - LDL value below 3.0 (- 2.5) mmol/L. Drug therapy is indicated if LDL does not decrease to below 3.0 with drugless therapy.
 - Serum triglyceride level below 2 mmol/L
 - Serum cholesterol/serum HDL below 5. Serum HDL in men > 0.9 and in women > 1.1
 - See related EBM Guideline: **Drug treatment for hyperlipidaemias** available on the EBM Web site for details on drug therapy.
- Treating obesity
 - Weight must be reduced to a target of BMI 28.
 - Recognize metabolic syndrome and consider starting combination therapy with a statin and fibrate.
- Physical exercise
 - Regular exercise improves the sense of well being and prognosis by reducing many risk factors (Level of Evidence=A; Evidence Summary available on the EBM Web site)

- Intense physical strain should be avoided.
 - On the basis of epidemiological studies, hormone replacement therapy has been considered beneficial for women with risk factors. A randomized secondary prevention study (HERS) did not, however, show any benefit from HRT (Level of Evidence=B; Evidence Summary available on the EBM Web site).
- Too hard physical or psychological stress may be dangerous. Psychosocial interventions (e.g. stress management training) are beneficial (Level of Evidence=A; Evidence Summary available on the EBM Web site).
- Age, male gender and family history of CHD are non-modifiable risk factors. They must be included in assessment of the total burden of risk factors.

Methods of action and treatment targets of pharmacotherapy

- Ischaemia is reduced by optimisation of blood pressure and heart rate. Beta-blockage is sufficient when heart rate is 60 - 50 bpm. The treatment of hypertension aims at an optimal pressure, which according to the HOT study² is 148/83 mmHg.
- ASA is not a symptom drug. It reduces the blocking of coronary arteries. ASA is recommended for all patients with ischaemic heart disease, unless contraindicated.
- Unstable angina (pre-infarction angina) must be treated urgently with ASA and LMW heparin, and revascularization should be planned.

Choosing the drug

- Sublingual "rapid" or aerosol nitrates that are classically used for acute episodes should also be used for prophylaxis.
- A selective beta-blocker reduces both heart rate and blood pressure. The target heart rate is about 60 bpm at rest and below 120 bpm during exercise. With age the dose can usually be reduced. Beta-blockers are first-line drugs also for the arrhythmias of IHD patients. Heart failure is not a contraindication. Carvediol may be the best choice in these cases. In heart failure an ACE inhibitor is usually combined with beta-blocker. Beta-blockers are not only a symptomatic therapy; they also reduce the risk cardiac infarctions and sudden deaths by 10 - 30%.
- Calcium antagonists may be used in case of adverse effects caused by beta-blockers. The most often used classic beta-blocker is diltiazem. Angina after a non-Q-wave infarction has been considered a special indication. New dihydropyridine derivatives (amlodipine, felodipine, isradipine, nisoldipine) can be combined with beta blockers in the treatment of stable AP particularly if hypertension is associated. The effect of calcium antagonists on prognosis is not documented as well as that of beta-blockers.
- Long-acting nitrates can be combined with a beta-blocker when the latter is not sufficient alone or used instead of beta-blocker when the drug is not tolerated. Nitrate is administered when symptoms occur, which is often daytime. The usual dose is 20 - 40 (- 60) mg/day. A nitrate patch can be used to treat nocturnal angina. The patch should be removed in the morning to avoid nitrate tolerance. For the same reason a pause should be kept in the administration of long-acting nitrates for example in the evening or at night. Nitrates are a symptomatic therapy and are not needed if the patient has no symptoms. They improve exercise tolerance but probably not the prognosis.
- The combination of beta-blockers, calcium antagonists and long-acting nitrates (triple therapy) is usually more harmful than beneficial.

- The survival-promoting effect of calcium antagonists after acute myocardial infarction is disputed (Level of Evidence=B; Evidence Summary available on the EBM Web site).

Revascularization

- Coronary artery bypass grafting (CABG)
 - Severe angina pectoris with associated three-vessel disease or occlusion of the proximal left anterior descending artery (LAD) that serves the anterior wall. Occlusion of the main left coronary artery (LCA) is an indication for surgery irrespective of the severity of symptoms ("widow maker")
 - A milder angina associated with left ventricle ischaemic ejection disturbance (EF < 50%) may be an indication for CABG. A deteriorated EF is often an additional indication not a contraindication.
 - Diabetic patients often benefit more from CABG than from PTCA.
 - Unstable angina associated with a small ejection fraction is often an indication for invasive treatment: CABG or PTCA.
 - In acute infarction, PTCA is often more readily available than CABG.
- Minimally invasive off-pump bypass grafting (Level of Evidence=C; Evidence Summary available on the EBM Web site). OP-CAB is a new surgical method that does not require the use of the heart-lung machine and thoracotomy.
- Percutaneous transluminal coronary angioplasty (PTCA)
 - Severe stable angina pectoris that responds poorly to medication.
 - Unstable angina particularly if response to medication is poor or the patient has a decreased exercise capacity or an elevated infarction marker.
 - A rapid recurrence of AP after CABG.
 - Severe AP in an elderly patient or a patient at risk.
 - Acute MI: a large infarction that does not respond to thrombolysis (rescue angioplasty) or the patient has a contraindication to thrombolysis and is at risk of a massive anterior infarction. Primary angioplasty is increasingly replacing thrombolysis, which is clearly not as efficient as angioplasty in opening the vessels. Long-term outcomes also continue to show the advantages of angioplasty over thrombolysis, largely because of stenting. However, the results obtained by thrombolytic therapy have also improved due to abciximab and other glycoprotein IIb/IIIa inhibitors.
 - PTCA is being used increasingly instead of CABG in the treatment of multi-vessel stable or unstable AP. Stents have improved the short- and long-term outcomes significantly (Level of Evidence=B; Evidence Summary available on the EBM Web site).

Related evidence

- Epidemiological studies suggest a reduction of cardiovascular risk associated with increased intake of vitamin E, but randomized controlled trials remain inconclusive (Level of Evidence=C; Evidence Summary available on the EBM Web site). Beta-carotene has not been shown beneficial in randomized trials, and it may be associated with increased risk of cancer.
- In patients with coronary disease, the use of short-acting nifedipine at moderate to high doses causes an increase in total mortality (Level of Evidence=C; Evidence Summary available on the EBM Web site).
- Beta-blockers and calcium antagonists provide similar outcomes, but beta-blockers may have fewer adverse effects (Level of Evidence=B; Evidence Summary available on the EBM Web site).

site).

- Dietary advice from health personnel is effective in achieving modest dietary change and cardiovascular risk reduction (Level of Evidence=B; Evidence Summary available on the EBM Web site).
- Compliance in the treatment of cardiovascular disease can be increased with several strategies. However, the quality of studies is suboptimal and no firm recommendations can be made of different strategies (Level of Evidence=B; Evidence Summary available on the EBM Web site).
- There is some weak evidence that fish consumption may reduce the risk of coronary death in high-risk populations, but probably not in low-risk populations (Level of Evidence=C; Evidence Summary available on the EBM Web site).
- Low cardiorespiratory fitness is a strong and independent predictor of CAD and all-cause mortality and comparable in importance with that of diabetes mellitus and other CAD risk factors (Level of Evidence=C; Evidence Summary available on the EBM Web site).

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